REMARKS

Reconsideration and withdrawal of the rejections of this application and consideration and entry of this paper are respectfully requested in view of the herein remarks and accompanying information, which place the application in condition for allowance.

1. Status of Claims and Formal Matters

Claims 48-71 are pending in this application. Claims 48-51 have been amended. Claim 68 has been cancelled. As will be discussed in detail in the next section, support for all of the pending claims and the claim amendments is found throughout the specification as originally filed. For example, support for the limitation "three-dimensional coordination geometry, which does not adsorb to apolar surfaces" is found, for example, in paragraph [0036] as published. No new matter has been added by this amendment.

The specification has been amended by adding a new paragraph after paragraph [0051] of published application US 2002/0149772 A1. Support for polydentate ligand is found in originally filed claim 24. Support for the various types of polydentate ligands is found in originally filed claim 25. Further support is found in Paragraphs [0043] and [0045]. Support for using stoichiometric or excess amounts of ligand is found in Paragraph [0039]. No new matter has been added.

It is submitted that the claims, herewith and as originally presented, are patentably distinct over the prior art cited by the Examiner, and that these claims were in full compliance with the requirements of 35 U.S.C. § 112. The amendments of the claims, as presented herein, are not made for purposes of patentability within the meaning of 35 U.S.C. §§§§ 101, 102, 103 or 112. Rather, these amendments and additions are made simply for clarification and to round out the scope of protection to which Applicants are entitled.

2 The Rejections Under 35 U.S.C. § 112 Are Overcome

Claims 48-71 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The Office Action points out that Applicants did not indicate where support for the claim amendments in the previous response can be found in the specification. However, it is noted that the amended claims were presented for clarification purposes, and that they mimicked the originally filed claims.

Claim 48 has been amended. The amended claim recites essentially the same method as originally filed claim 1. Furthermore, support for claim 48 can be found throughout the originally filed specification. In particular, referring to published application US 2002/0149772 A1, paragraphs 45-46 support the general steps in the method claim. Support for claim 48 is also found in the abstract and in paragraph 2 of the specification.

The Office Action contends that there is no support for the term "polydentate ligand" in the specification. However, the originally filed claims are considered part of the specification. Originally filed claims 24 and 25 clearly indicate that the ligand which complexes to the indicator ions is a polydentate ligand. Applicants respectfully remind the examiner that the claims as filed in the original specification are part of the disclosure and therefore, if an application as originally filed contains a claim disclosing matter not disclosed in the remainder of the specification, the applicant may amend the specification to include the claimed subject matter. *In re Benno*, 768 F.2d 1340, 226 USPQ 683 (Fed. Cir. 1985).

Moreover, paragraph 23 points out several examples of polydentate ligands that can be used in this invention The Examples described in paragraphs 43-50 make use of a polydentate ligand. Figures **2a** and **3a** display specific examples of polydentate ligands which are used in preferred embodiments of the present invention. It is noted that the term polydentate ligand refers to a ligand that is attached to a central metal ion by bonds from two or more donor atoms. Given the explicit mentioning of polydentate ligands in the originally filed claims, the references to multiple polydentate ligands in the specification, and the diagrams depicting polydentate ligands, one of ordinary skill in the art certainly would conclude that Applications had possession of methods of measuring the volume of liquid samples employing polydentate ligands.

Support for the remaining claims can be found throughout the originally filed specification. The other independent claims are variations of claim 48. Claim 49 corresponds to originally filed claim 2. Claims 50 and 51 correspond to originally filed claims 2 and 3. It is further noted that apart from the claims to which they depend, the dependent claims are nearly identical to the originally filed dependent claims. For instance, claim 52 corresponds to originally filed claim 5. Claim 53 corresponds to originally filed claim 5. Claim 54 corresponds to originally filed claim 8. Claim 54 corresponds to originally filed claim 8. Further support for claim 54 is found in paragraph 38. Claim 55 corresponds to originally filed claim 9. Claim 56

corresponds to originally filed claim 11. Claim 57 corresponds to originally filed claims 24 and 25. Claims 58-60 correspond to originally filed claims 13-15. Claims 61-62 correspond to originally filed claims 22-23. Claims 63-67 correspond to originally filed claims 25-29. Support for claims 68 and 70 can be found in Paragraph 36 of the originally filed application. Support for claim 71 can be found in Paragraph 40 of the originally filed application.

Consequently, reconsideration and withdrawal of the Section 112 rejection is earnestly requested.

3 The Rejections Under 35 U.S.C. § 103 Are Overcome

Claims 48-63 and 66-71 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent No. 5,061,639 to Lung *et al.* (hereinafter "Lung") in view of U.S. Patent No. 5,320,969 to Bauer *et al.* (hereinafter "Bauer"). These rejections are respectfully traversed. The cited references do not make the instant invention obvious.

The Examiner is respectfully directed to the case law, namely, that there must be some prior art teaching which would have provided the necessary incentive or motivation for modifying the reference teachings. *In re Laskowski*, 12 U.S.P.Q. 2d 1397, 1399 (Fed. Cir. 1989); *In re Obukowitz*, 27 U.S.P.Q. 2d 1063 (BOPAI 1993). Further, as stated by the Court in *In re Fritch*, 23 U.S.P.Q. 2d 1780, 1783-1784 (Fed. Cir. 1992): "The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggests the desirability of the modification." For the §103 rejection to be proper, both the suggestion of the claimed invention and the expectation of success must be founded in the prior art, and not Applicant's disclosure. *In re Dow*, 5 U.S.P.Q.2d 1529, 1531 (Fed.Cir. 1988).

Applying the law to the instant facts, the reference relied upon by the Office Action does not disclose, suggest or enable Applicant's invention. Lung and Bauer, alone or in combination, do not disclose, suggest or enable the presently claimed invention.

The three-dimensional coordination geometry of the complex pigment is a very important feature of the present invention (see, e.g., paragraph 36 of the application as published). The present invention satisfies a long felt need for a more reliable means for measuring the quantity of dispensed droplets (see, e.g., paragraphs 11-14 of the application as published). Specifically,

the three dimensionality of the complex allows a user to accurately determine extremely small volumetric measurements with a high degree of accuracy.

In contrast, the labels of Bauer exhibit a planar coordination geometry that are not suitable for the purposes of the present invention. Even assuming, arguendo, that one of skill in the art had selected some of the Bauer labels for use in the method of Lung, one of skill in the art would not have restricted the selection on complexes with a three-dimensional coordination geometry that greatly hinders the adsorption of this type of molecule to apolar surfaces.

Referring to independent claim 48, there are several important limitations not found in Lung. Lung does not teach "providing a diluent comprising polydentate chromogenic ligands." Lung does not teach or suggest using a chromophoric indicator that has "a three-dimensional geometry." Lung does not teach "dispensing a volume of the sample liquid containing a fixed concentration of indicator ions into the solution." Moreover, Lung does not use a calibration curve in making volumetric determinations.

Notably, Lung directly pipettes the colorimetric reagent into the well rather than pipetting indicator ions which complex to polydentate ligands. As pointed out in paragraphs 11-14 of the Applicant's specification, such a technique does not allow one to measure very small volumes in the nanoliter range. Moreover, the only two examples of colorimetric reagents disclosed in Lung, cobalt sulfate and potassium dichromate, are not capable of being used to measure small volumes of liquid in the nanoliter range for reasons already stated on record.

Bauer does not cure the deficiencies in Lung. Bauer merely recites that metal ions in urine samples will displace a polyvalent metal ion from the indicator molecule resulting in a color change. The color change provides a semiquantitative means of determining the specific gravity of a test sample, such as urine. Because Bauer's method relies on a color change, the colored ligand/metal ion complex is pre-formed in the test chamber. Subsequently, a second metal ion is added to displace the first metal ion in the complex, thus resulting in the color change. In claim 48 of the pending application, a ligand/metal complex is formed only after the addition of indicator ions. The solution, initially clear, changes color following the addition of the indicator ions to the diluent containing a polydentate ligand. Thus, the step of forming the chromophoric indicator to stain the mixture is not taught or suggested in Bauer. It is further noted that in column 12, lines 1-2 of Bauer, Bauer indicates that the "color transition usually is a decrease in color intensity and degree." This statement directly contrasts with the invention

application where the intense color development following addition of indicator ions enables the determination of very small volumes of dispensed liquid samples with high accuracy.

Clearly, the combination of Lung and Bauer does not teach every element of claim 48. Furthermore, as the remaining independent claims are modifications of claim 48, the same arguments apply with respect to these claims. For instance, claim 49 is directed to determining the residual volume of a liquid sample by a method similar to that recited in claim 48. In addition to the missing limitations already discussed in Lung and Bauer, there is no teaching or suggestion in either of the references regarding determining residual volumes in sample chambers.

With respect to claims 50 or 51, neither Bauer nor Lung teach or suggest "dispensing a volume of a liquid sample" of a chromophoric indicator which is a "polydentate ligand with a three-dimensional geometry, which does not adsorb to polar surfaces." As discussed above, Lung dispenses either cobalt sulfate or potassium dichromate into the diluent. Bauer does not dispense any chormophoric ligand into a diluent, but rather dispenses metal ions into a diluent. Thus, the combination of Lung and Bauer do not teach or suggests either claims 50 or 51.

In previous responses, the Applicant has established that there is no motivation in either Bauer or Lung to combine the references. These arguments are summarized below.

Lung does not provide any motivation to replace cobalt sulfate or potassium dichromate with polydentate chromogenic ligands that have a three-dimensional geometry. Lung does not allude to any deficiencies with using cobalt sulfate as a colorimetric reagent. For instance, Lung does not suggest that extremely high concentrations of cobalt sulfate would need to be used to determine small volumes in the nanoliter range. Lung also does not teach or suggest that such high concentrations of colorimetric reagent would change the properties of the aqueous solution, thus precluding accurate volumetric determinations. In fact, there is no indication in Lung that the method disclosed can be used to measure extremely small volumes, as in the present invention. Lung only indicates that his liquid dispensing method can be used to measure volumes in the μL range (refer to paragraph 2, lines 7-16, and the table in column 5 of Lung). Finally, with respect to claims 48 and 49 of the pending application, Lung gives no motivation for pipetting indicator ions rather than chromogenic ligands, which stick to the walls of a pipette when used in high concentrations.

Bauer also does not provide any explicit or implicit motivation to combine with Lung. As noted in the previous response, although some polydentate ligands are mentioned in Bauer, essentially every known indicator that binds to a polyvalent metal ion are provided as examples of potential colorimetric reagents (see e.g., col. 12, line 54 through col. 13, line 20). In addition, there is no actual preference by Bauer that would direct a reader to the indicator molecules claimed in the present application. In fact, Bauer states that "the indicator can be essentially any compound, such as a dye, that interacts with the polyvalent metal ion-indicator complex." (Column 12, lines 16-19).

Thus, there is absolutely no motivation to combine the disclosures of Lung and Bauer. The Office Action states, however, "that the motivation to combine references is not requires to be directed to solve the problem or achieve the same goals as that desired by applicant." However, the Examiner did not provide any motivation at all to combine Bauer and Lung. Moreover, the Examiner did not point out any particular advantage suggested in Bauer or Lung that would motivate one of ordinary skill in the art to combine the two references. Thus, it is respectfully asserted that the Examiner is using improper hindsight based on the Applicant's disclosure. The Applicant reminds the Examiner that it is impermissible to engage in a hindsight reconstruction of the claimed invention, using the Applicant's structure as a template, and selecting elements from references to fill in the gaps. *Interconnect Planning*, 744 F.2d 1132, 1143 (Fed. Cir. 1985).

Consequently, reconsideration and withdrawal of the Section 103 rejections are earnestly requested.

REQUEST FOR AN INTERVIEW

If any issue remains as an impediment to allowance, a further interview with the Examiner and SPE are respectfully requested and the Examiner is additionally requested to contact the undersigned to arrange a mutually convenient time and manner for such an interview.

CONCLUSION

In view of the remarks, the application is believed to be in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are earnestly solicited. The undersigned looks forward to hearing favorably from the Examiner at an early date, and, the Examiner is invited to telephonically contact the undersigned to advance prosecution.

Respectfully submitted,
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